Original Article

A comparative study on the efficacy of dexmedetomidine and tramadol on post-spinal anesthesia shivering

ABSTRACT

Background: Shivering is a common postanesthesia adverse event with multiple etiologies. At present tramadol is a widely used drug for the control of shivering. However, tramadol may cause a lot of nausea and vomiting. Hence, the need to find a better drug with less of side effects. The aim of this study was to compare the efficacy of dexmedetomidine and tramadol in the treatment of post-spinal anesthesia (SA) shivering as well as to compare their side-effect profile.

Materials and Methods: This prospective, double-blind, randomized controlled trial was conducted in a tertiary care hospital. A total of 100 patients having shivering after SA were enrolled, out of which fifty received dexmedetomidine (Group A) and 50 received tramadol (Group B). The response rate, time to cessation of shivering and side effects (if any) was noted. All the results were analyzed using Student's *t*-test and Chi-square test.

Results: All patients who received dexmedetomidine as well as tramadol had cessation of shivering. The time to cessation of shivering was significantly less with dexmedetomidine (174.12 ± 14.366 s) than with tramadol (277.06 ± 23.374 s) ($P < 0.001$). The recurrence rate of shivering with dexmedetomidine was less (6%) as compared to tramadol (16%). Nausea and vomiting was found to be higher in the case of tramadol. On the other hand, dexmedetomidine caused moderate sedation (modified Ramsay sedation score = 3–4) from which the patient could be easily awoken up.

Conclusion: Dexmedetomidine offers better results than tramadol with fewer side effects.

Key words: Dexmedetomidine; postoperative nausea and vomiting; shivering; tramadol

Introduction

Shivering is defined as an involuntary, repetitive activity of skeletal muscles. It is a common postanesthesia adverse event with an incidence of 40–70%.[1] Various mechanisms have been suggested for postanesthesia shivering. These include intraoperative heat loss, postoperative increased sympathetic tone, pain and systemic release of pyrogens.[2] Though hypothalamic thermoregulation remains intact during regional anesthesia, it is associated with greater heat loss than general anesthesia which is attributed to various reasons like abnormal heat loss due to vasodilatation, impairment of shivering in the area of block and rapid intravenous (IV) infusion of cold fluids.[3]

Shivering is not only physically distressing for the patient, but can have various other detrimental effects. It may lead to pain, patient discomfort, impede monitoring techniques, increase intraocular and intracranial pressures, double or even triple oxygen consumption and carbon dioxide

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production,[4] which might pose difficulties in patients with existing intrapulmonary shunts, fixed cardiac output or limited respiratory reserve.

Various modalities have been used for the prevention and treatment of postanesthesia shivering. Dexmedetomidine, a centrally acting alpha 2-adrenergic agonist, has been used as a sedative agent and is known to reduce the shivering threshold. Various studies have been performed using dexmedetomidine in the prophylaxis of postoperative shivering.[5] But until date, there are limited studies using dexmedetomidine in the treatment of postoperative shivering.

Tramadol, an opioid receptor agonist, is an inhibitor of the re-uptake of serotonin (5-hydroxytryptamine) and norepinephrine in the spinal cord. This facilitates 5-hydroxytryptamine release, which influences thermoregulatory control. Presently it is a widely used drug for the control of shivering. But tramadol may cause nausea and vomiting which is very distressing for the patient. Hence the need to find a better drug which has comparable efficacy to tramadol and at the same time has less of side effects. The aim of the study was to compare the efficacy of dexmedetomidine and tramadol in the treatment of post-spinal anesthesia shivering as well as their side-effect profile.

Materials and Methods

The present study was a prospective, double-blind, randomized controlled trial conducted on 100 American Society of Anesthesiologists (ASA) Grade I/II adult patients (>18 years) having shivering during surgeries under spinal anesthesia (SA) out of which fifty received dexmedetomidine (Group A) and 50 received tramadol (Group B). The sample size was determined keeping the value of alpha (α) = 0.05 and beta (β) = 0.2. We hypothesized that the test drug will be significantly better if it decreased the time taken to abolish shivering by 1 min as compared to control group drug (tramadol). We took the maximum standard deviation (SD) which was 1.69 as per previous study.[6] Applying the formula for a two-sided study:

n (size per group) $= 2c/\delta^2 + 1$

where, $\delta = (\mu 2 - \mu 1)/\sigma$ is the standardised effect size

$\mu 1$ and $\mu 2$ are the means of the two treatment groups

σ is the common SD

$c = 7.9$ for 80% power

Hence, $n = 2 \times 7.9/(1/1.69)^2 + 1 = 46.1$.

Rounding off, we took the sample size as 50 per group.

Patients with coagulopathy, elderly (age >65 years), bradycardia (heart rate [HR] <60/min), heart blocks, pregnant and nursing mothers or allergy to drugs used or to the drug group were excluded from the study.

Patients were randomly allocated to Group A or Group B on the basis of computer-generated random table. The randomization scheme was generated using the Website Randomization.com (http://www.randomization.com). The computer generated Group number (A or B) was put in a closed opaque envelope. A person not related to study (anesthesia nurse) was asked to open the closed envelope containing computer generated group number on start of shivering in the patient. She prepared the drug in 50 ml syringe and sent it for use without labelling which drug it was, but she kept a record of the same. If the second dose of the drug was required, she again sent it in an unlabelled syringe. The administering anesthesiologist was not knowing which drug was being given. He would fill up the study proforma noting down the various parameters, and this proforma would be collected again by the anesthesia nurse who would put it back in the torn envelope. At the end of the study, these envelopes were handed to the principal investigator.

All patients were monitored by noninvasive blood pressure (NIBP), pulse rate, SpO_2 and axillary temperature.

Initiation of subarachnoid block was done by injection bupivacaine (0.5%) at L2-3 or L3-4 interspace. There was no active warming of patients and the fluids were used at room temperature. The room temperature in the entire operation theater complex, pharmacy area and surgical recovery room was kept constant between 21 and 24°C. Vitals including NIBP, pulse rate, SpO_2 and axillary temperature were recorded in the beginning of the surgery and at the onset of shivering from the monitoring chart, after cessation of shivering and then every 10 min till the end point of study.

- In Group A: Dexmedetomidine (0.5 mcg/kg) in the concentration of 1 mcg/ml was given over 10 min if there was shivering in patient after initiation of subarachnoid block
- In Group B: Tramadol (0.5 mg/kg) in the concentration of 1 mg/ml was given over 10 min, if there was shivering in patient after initiation of subarachnoid block.

Grading of shivering was done as follows:

- Grade 0: No shivering
- Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscle activity
- Grade 2: Visible muscle activity confined to one muscle group

- Grade 3: Visible muscle activity in more than one muscle group
- Grade 4: Gross muscle activity involving the whole body.

Patients who developed either Grade 3 or Grade 4 of shivering were included in the study. Same criteria were used for grading shivering during recurrence and patients with Grade 3 or 4 shivering were included.

The attending anesthesiologist would record:

1. The time at which shivering started after SA (onset of shivering) and the time of recurrence, if present (defined as the time between cessation of shivering after the first dose of the drug and recurrence of shivering)
2. Severity of the shivering
3. Response rate (number of patients in which shivering ceased after treatment in 15 min)
4. Time to disappearance of shivering (in seconds).

The total duration of surgery was noted and the duration of SA was recorded by assessing spontaneous recovery of sensory block using pin-prick method and observing spontaneous movements of limbs in the postoperative period. If the shivering did not subside by 15 min, the treatment was considered to be not effective. Recurrence of shivering was also noticed. Patients who did not respond or in whom recurrence of shivering occured were treated with additional dose of dexmedetomidine (0.25 μg/kg IV) or tramadol (0.25 mg/kg IV) in the respective groups. If some patients did not respond to the additional dose, they would be regarded as treatment failure. This would be used to calculate the response rate. Side effects like nausea, vomiting, itching, bradycardia (<60/min), hypotension (decrease >20% of baseline of systolic blood pressure/diastolic blood pressure [SBP/DBP]) and sedation score were recorded.

Sedation score was assessed as per modified Ramsay score:

Grade	Patient response
1	Anxious, agitated, restless
2	Cooperative, oriented, tranquil
3	Responds to commands only
4	Brisk response to light glabellar tap or loud noise
5	Sluggish response to light glabellar tap or loud noise
6	No response

Bradycardia, hypotension, and vomiting were treated with Inj atropine 0.6 mg i/v, Inj ephedrine in 6 mg boluses i/v titrated until blood pressure (BP) reached within 20% of baseline BP and Inj metoclopramide 10 mg i/v, respectively, when required.

Postoperatively, after shifting patients to postanesthesia care unit (PACU), patients were not actively warmed and were given fluids at room temperature.

The end point for the study was either sensory (using pin-prick method) and motor recovery from subarachnoid block or the patient was given either of the two drugs twice for the treatment of shivering.

For motor recovery from subarachnoid block, the Bromage scale was used as per institutional practice which is as under:

- Bromage 3: Unable to move feet or knees
- Bromage 2: Able to move feet only
- Bromage 1: Just able to move knees
- Bromage 0: Full flexion of knees and feet.

All the results were analyzed using Student's *t*-test and Chi-square test. Data were expressed as mean ± SD or percentage. A $p < 0.05$ was considered statistically significant. A $p < 0.001$ was considered highly significant.

Results

The incidence of shivering in our study came out to be 41%. Written informed consent was taken from 244 patients undergoing various surgeries under SA, until the time 100 patients developed shivering and were enrolled in the study. The consort diagram is shown in Figure 1.

Both the groups were comparable with respect to sex, age, weight, ASA grade, duration of surgery, type of procedure done and the duration of spinal block [Tables 1 and 2].

The ambient temperature of the operation theatre in Group A was 21.56 ± 0.577°C while in Group B it was 21.60 ± 0.606°C ($P = 0.736$). Similarly, ambient temperature of recovery room in Group A was 23.62 ± 0.490°C while in Group B it was 23.60 ± 0.495°C ($P = 0.840$).

Shivering disappeared in 100% patients who received dexmedetomidine and tramadol. Both the drugs were found to be effective in reducing shivering.

Three patients in Group A (6.00%) and eight patients (16.00%) in Group B had recurrence of shivering and were given second doses of dexmedetomidine or tramadol, respectively ($P = 0.110$).

Shivering disappeared in 100% patients who received the second dose of dexmedetomidine and tramadol.

Time for onset of shivering and severity of shivering were not statistically significantly different between

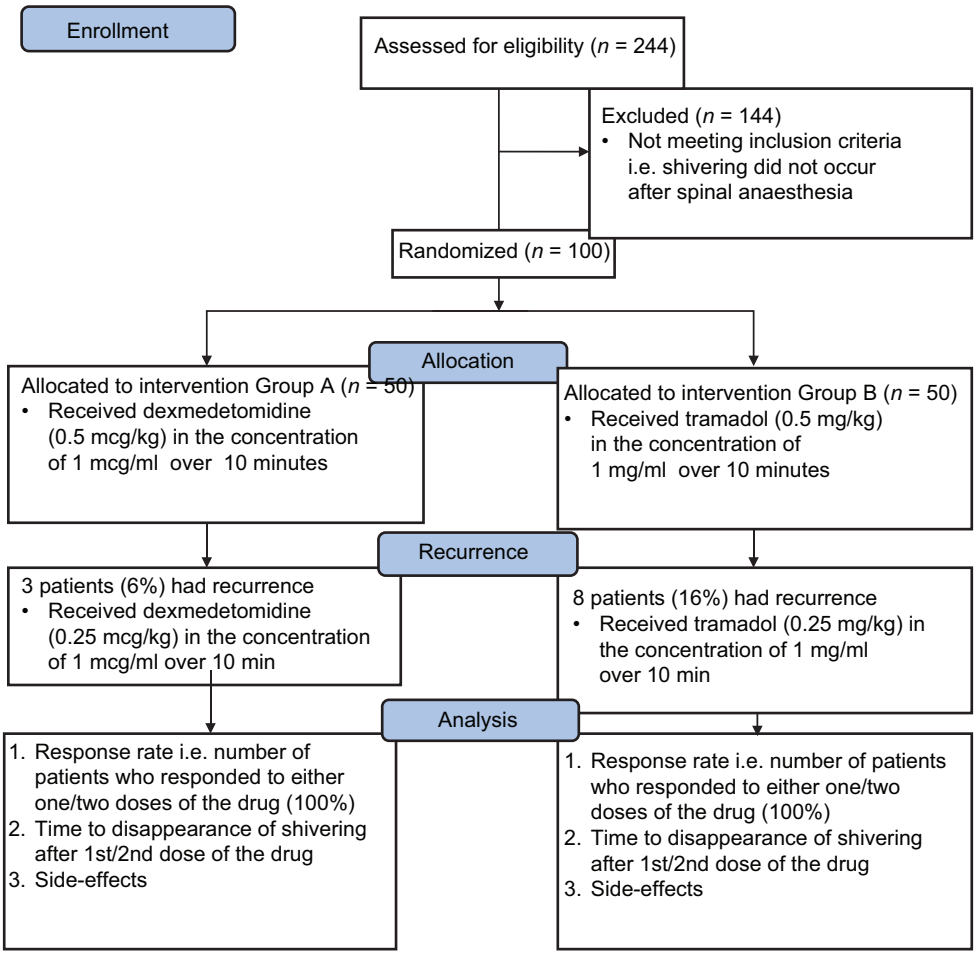

Figure 1: Consort transparent reporting of trials CONSORT 2010 flow diagram

Table 1: Demography of the two study groups

	Sex		Age (years)	Weight (kg)	ASA grade		Duration of surgery (min)	Duration of spinal anesthesia (min)
	Male	Female			I	II		
Dexmedetomidine	27	23	49.80±12.025	74.60±9.258	25	25	78.72±30.080	121.90±29.964
Tramadol	25	25	45.98±13.003	73.94±9.429	20	30	86.70±35.020	132.30±31.360
P	0.689		0.130	0.725	0.315		0.225	0.093

ASA: American Society of Anesthesiologists

the two groups. Similarly, the time of recurrence of shivering, whenever it occurred was comparable in the two groups. The mean interval between the injection of drug (dexmedetomidine and tramadol) and the complete cessation of shivering was significantly lesser in the dexmedetomidine group [Table 3].

There was no statistically significant difference with respect to SBP/DBP, axillary temperature, and oxygen saturation between the two groups [Figures 2a and b, 3, 4].

There was no statistically significant difference with respect to baseline HR and HR at the onset of shivering. However, the HR decreased significantly in Group A as compared to Group B immediately after cessation of shivering. There was no statistically significant difference with respect to HR at all other time intervals [Figure 5].

Complication rates were significantly higher in Group B than in Group A. Nausea and vomiting were higher in Group B than in Group A. 28.00% patients in Group B had nausea compared to none in Group A with a highly significant $P < 0.001$. Furthermore, 8.00% patients in Group B had vomiting compared to none in Group A with a significant $P = 0.041$.

None of the patients in either group had itching and hypotension while one patient in Group A had bradycardia. No patient in Group B had bradycardia ($P = 0.315$).

Table 2: Distribution of patients according to the type of procedure done in the two study groups

Procedure	Group (%)		Total (%)	*P*
	Dexmedetomidine	Tramadol		
EUA + fistulectomy for fistula-in-ano	3 (6.00)	1 (2.00)	4 (4.00)	0.962
Excision of pilonidal sinus and flap coverage	1 (2.00)	2 (4.00)	3 (3.00)	
Foot surgery	1 (2.00)	1 (2.00)	2 (2.00)	
Haemorrhoidectomy	1 (2.00)	1 (2.00)	2 (2.00)	
Inguinal hernioplasty	2 (4.00)	2 (4.00)	4 (4.00)	
laparotomy for ectopic pregnancy	1 (2.00)	0 (0.00)	1 (1.00)	
LSCS for IUD	1 (2.00)	1 (2.00)	2 (2.00)	
Orthopaedic surgery other than TKR and THR	15 (30.00)	15 (30.00)	30 (30.00)	
Scrotal surgery	1 (2.00)	1 (2.00)	2 (2.00)	
Stripping of varicose veins	1 (2.00)	0 (0.00)	1 (1.00)	
Suturing lower limb	1 (2.00)	1 (2.00)	2 (2.00)	
TAH with BSO	3 (6.00)	6 (12.00)	9 (9.00)	
THR	3 (6.00)	1 (2.00)	4 (4.00)	
TKR	11 (22.00)	9 (18.00)	20 (20.00)	
TURP	1 (2.00)	1 (2.00)	2 (2.00)	
URSL	2 (4.00)	6 (12.00)	8 (8.00)	
Vaginal hysterectomy	2 (4.00)	2 (4.00)	4 (4.00)	
Total	50 (100.00)	50 (100.00)	100 (100.00)	

EUA: Examination under anesthesia; IUD: Intrauterine death; LSCS: Lower segment caesarean section; TKR: Total knee replacement; THR: Total hip replacement; BSO: Bilateral salpingo-oophorectomy; TURP: Transurethral resection of the prostate; URSL: Ureterorenoscopic lithotripsy

Table 3: Comparison of the time of onset of shivering, severity of shivering, time to disappearance of shivering, and time of recurrence in the two study groups

	Dexmedetomidine	Tramadol	*P*
Time of onset of shivering (min)	72.30±41.357	72.66±41.640	0.965
Severity of shivering	3.92±0.274	3.96±0.198	0.405
Time to disappearance of shivering (s)	174.12±14.366	277.06±23.374	<0.001
Time of recurrence (min)	70.00±17.321	73.75±21.171	0.792

Patients of Group A were more sedated than of Group B. While 14 (28.00%) patients in Group A had Grade 3 sedation score, 36 (72.00%) patients had sedation of Grade 4. On the other hand, all the patients in Group B had a sedation of Grade 2 ($P < 0.001$).

Discussion

Shivering is known to be a frequent complication in patients undergoing surgery under neuraxial anesthesia. Shukla *et al*.[1] have reported the incidence of shivering in patients undergoing surgery under regional anesthesia at 40–70% based on previous studies. The incidence of shivering in our study was 41%.

In this study, we studied the efficacy of dexmedetomidine in the treatment of post-SA shivering in adults and compared its efficacy with tramadol for the treatment of shivering after SA in patients undergoing various elective surgeries.

Although tramadol is an established drug in the treatment of shivering, in this study, we found that dexmedetomidine is equally effective as tramadol in treating post-SA shivering.

The efficacy of dexmedetomidine is similar to that of a previous study by Blaine Easley *et al*.[7] who studied the role of dexmedetomidine in the treatment of postoperative shivering in children. All children had a cessation of shivering behavior within 3.5 ± 0.9 min, while in our study cessation of shivering occurred in 2.9 ± 0.23 min (174.12 ± 14.366 s). This difference could be due to different methodology used to see the time for cessation of shivering. While Blaine Easley *et al*. recorded their results as the number of patients who had stopped shivering after 1 min, after 2 min and so on, and then extrapolated the time taken for cessation of shivering from these data. However, in our study, we directly observed the time taken for shivering to stop (in seconds). Second, while Blaine Easley *et al*. studied a small sample size of 24 patients, we had taken a much larger sample size of 50 patients. There is limited data where researchers have looked for time for cessation of shivering with dexmedetomidine.

In this study, the cessation of shivering with tramadol occurred in 277.06 ± 23.374 s (4.61 ± 0.38 min). This is in accordance with previous literature.[1]

There is a paucity of literature comparing the efficacy of dexmedetomidine with tramadol. However, from our study, we found that the time interval from the administration of treatment to cessation of shivering is significantly less with dexmedetomidine (174.12 ± 14.366 s) than with tramadol (277.06 ± 23.374 s) ($P < 0.001$).

Six percent patients in dexmedetomidine group in the present study had recurrence of shivering. However, none of the patients had recurrence of shivering after receiving dexmedetomidine in earlier study conducted by Blaine Easley *et al*.[7] This could be due to the fact that in the study conducted by Blaine Easley *et al*. the surgeries were conducted under general anesthesia, while in our study the surgeries were performed under SA. While in general anesthesia patients, shivering occurs only on awakening, in SA patients it can occur at any time post-SA. This may lead to a higher incidence of shivering and recurrence of shivering in patients undergoing SA as compared to patients undergoing surgeries under general anesthesia.

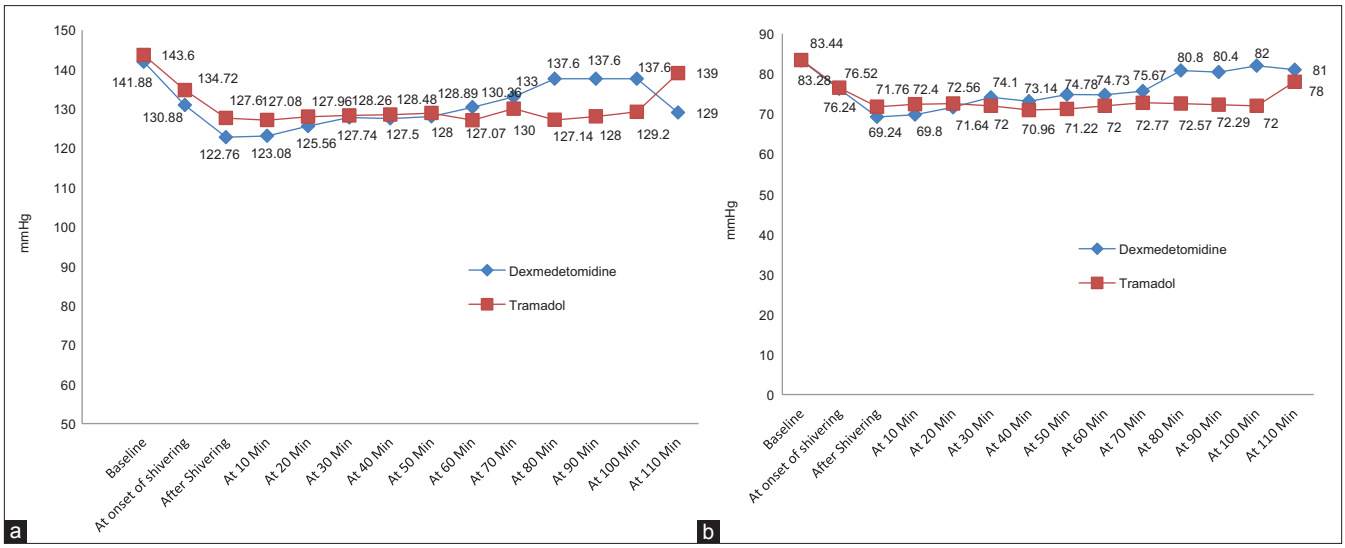

Figure 2: (a) Comparison of systolic blood pressure at various time intervals in the two groups. (b) Comparison of diastolic blood pressure at various time intervals in the two groups

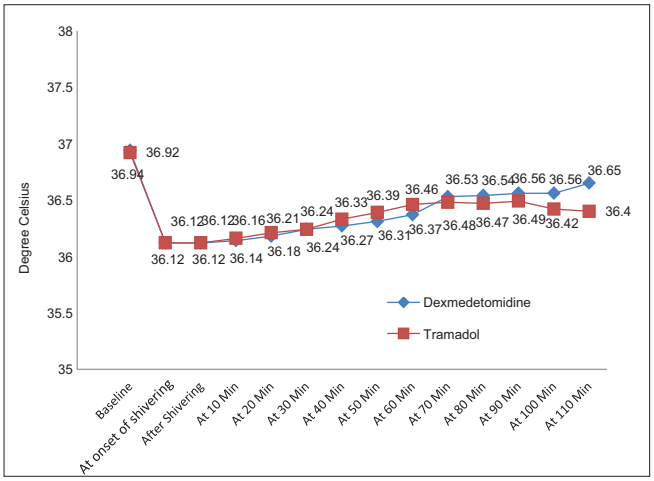

Figure 3: Comparison of axillary temperature at various time intervals in the two groups

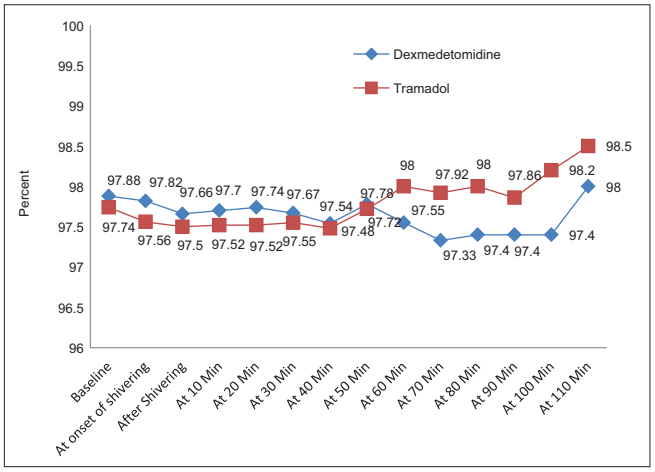

Figure 4: Comparison of SpO_2 at various time intervals in the two groups

The difference could also be due to the fact that the patients studied in Easley's study were children in the age group of 7–16 years. The incidence of shivering has been reported to be less in children as compared to adults.[8] To date, there have been very few studies regarding the treatment of shivering in children. Hence, it is quite difficult to interpret data regarding recurrence of shivering after administration of pharmacological treatment from the limited number of available studies.

The third reason for the difference in the recurrence rate between Easley's study and our present study could be due to their small sample size in which they studied only 24 children. Our sample size ($n = 50$) was nearly double than their sample size.

About 16% patients who received tramadol in our study had recurrence of shivering. This incidence was similar to available literature.[9]

In this study, the incidence of recurrence of shivering with dexmedetomidine was less (6%) as compared to tramadol (16%), but the difference was not statistically significant ($P = 0.110$).

The side effects were found to be higher in the case of tramadol as compared to dexmedetomidine. In this study, the incidence of nausea was highly significant in tramadol group compared to the dexmedetomidine group ($P < 0.001$). Similarly, the incidence of vomiting was significantly higher in the tramadol group compared to dexmedetomidine group ($P = 0.041$).

Postoperative nausea and vomiting (PONV) is a very unpleasant experience for the patient. Postoperative vomiting/retching can lead to rare but serious medical complications, such as aspiration of gastric contents, suture dehiscence, esophageal rupture, subcutaneous emphysema, or pneumothorax. PONV

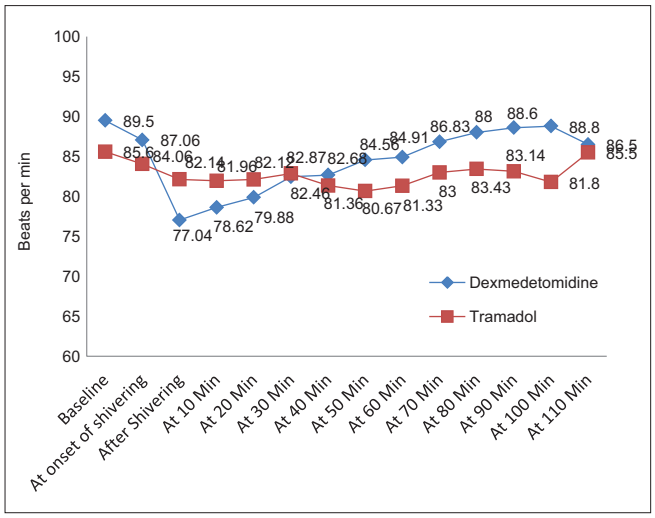

Figure 5: Comparison of pulse rate at various time intervals in the two groups

may delay discharge from PACUs and can be the leading cause of unexpected hospital admission after ambulatory anesthesia.[10]

One patient in the dexmedetomidine group of our study had bradycardia while none in the tramadol group had bradycardia. However, the incidence was not statistically significant ($P = 0.315$). Although dexmedetomidine decreases the HR significantly immediately after cessation of shivering, the incidence of bradycardia (HR <60/min) is not significant. The fall in HR immediately after cessation of shivering in Group A is due to the inherent property of dexmedetomidine to decrease HR due to postsynaptic activation of α_2 adrenoceptors in the central nervous system. Gradually, the HR picked up in Group A and was comparable in the two groups at all other time intervals.

In our study, 28% patients of dexmedetomidine group exhibited a Ramsay Sedation Score of 3, while 72% patients had a Ramsay sedation score of 4. However, the level of sedation in these patients never went above Grade 4, and these patients were able to maintain their airway and SpO_2 on room air. There was no incidence of hypoxia in our study consequent to the loss of airway due to deeper planes of sedation. This sedation was found to be beneficial in the post-SA patients who were more comfortable in the recovery room with some amount of sedation from which they could be easily awoken.

There was no incidence of hypotension in either group, which is similar to previous studies.[1,7] Similarly, none of the patients in either group had itching.

On overall analysis, more side effects were noted in tramadol group patients compared to dexmedetomidine group patients.

A limitation of this study is that we could not measure the core body temperature. For measurement of core body temperature, the probe needs to be put in the mid-esophagus or near the tympanic membrane or in the urinary bladder. While a probe in the mid-esophagus or near the tympanic membrane is uncomfortable and unacceptable for patients who have been given SA, a probe in the urinary bladder would be an undue source of infection for the patient. Axillary temperature was recorded at regular intervals perioperatively until the end of the study.

Conclusion

Dexmedetomidine is a useful alternative to tramadol for cessation of post-SA shivering. Nausea and vomiting are lesser whereas it provides faster relief from shivering.

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Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. Indian J Anaesth 2011;55:242-6.
2. Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med 2008;33:241-52.
3. Chaturvedi S, Domkondwar G. Control of shivering under regional anaesthesia using tramadol. Asian Arch Anaesthesiol Resusc 2002;57:491-6.
4. De Witte J, Sessler DI. Perioperative shivering: Physiology and pharmacology. Anesthesiology 2002;96:467-84.
5. Usta B, Gozdemir M, Demircioglu RI, Muslu B, Sert H, Yaldiz A. Dexmedetomidine for the prevention of shivering during spinal anesthesia. Clinics (Sao Paulo) 2011;66:1187-91.
6. Sajedi P, Khalili G, Kyhanifard L. Minimum effective dose of tramadol in the treatment of postanesthetic shivering. J Res Med Sci 2008;13:75-9.
7. Blaine Easley R, Brady KM, Tobias JD. Dexmedetomidine for the treatment of postanesthesia shivering in children. Paediatr Anaesth 2007;17:341-6.
8. Akin A, Esmaoglu A, Boyaci A. Postoperative shivering in children and causative factors. Paediatr Anaesth 2005;15:1089-93.
9. Joshi SS, Arora A, George A, Shidhaye RV. Comparison of intravenous butorphanol, ondansetron and tramadol for shivering during regional anesthesia: A prospective randomized double-blind study. Anaesth Pain Intensive Care 2013;17:33-9.
10. Apfel CC. Postoperative nausea and vomiting. In: Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anaesthesia. 7th ed. New York: Churchill Livingstone; 2010.